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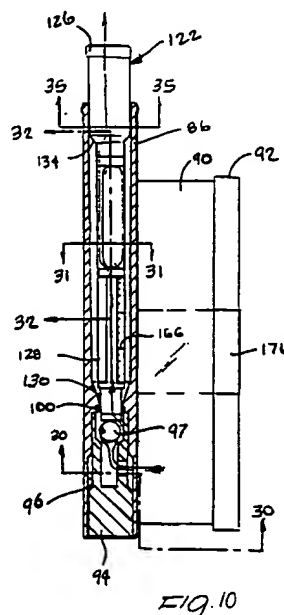
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(54) **Breath-sampling device for measuring breath component levels.**

(57) The present invention relates to devices, kits and disposable columns for use in such kits for monitoring levels of various components in the breath of a user. The device generally comprises a) an outer tubular member (86) having an open first end and a second end; b) valve means (94,97) disposed toward the second end of said outer tubular member; c) a breath sample collection means having one end mounted on said tubular member and having the other end closed, and having an interior in communication with the inside of said outer tubular member (86) through said valve means (94,97); and d) a disposable tubular analyzer column (122) having a mouthpiece (126) and containing material reactive to the presence of said breath components, wherein said column (122) is insertable into said outer tubular member (86) and cooperates with said valve means (94,97) to permit breath blown by a user to pass through the outer tubular member (86) into said sample collection means and to permit said collected breath sample to discharge through the reactive material of said analyzer column (122).

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The present invention relates to devices, kits and disposable columns for use in such kits for monitoring levels of various components in the breath of a user. The devices, kits and disposable columns of the invention contain material reactive to the presence of said breath components. The devices, kits and disposable columns of the invention may be useful, for example, in the quantitative determination of ketone and aldehyde, in particular acetone, concentrations for the purpose of monitoring the effects of diet, exercise and diabetic conditions.

It is well known in the art that breath samples may be assayed for the presence of acetone in order to determine serum acetone levels. Acetone is a relatively volatile compound having a partition coefficient of approximately 330. It readily diffuses from the blood into the alveolar air of the lungs according to an equilibrium relationship. As a consequence of this equilibrium state, concentrations of acetone in alveolar air are directly proportional to those in the blood and measurements of acetone in alveolar air can be used to determine the concentration of acetone in the serum. Crofford, *et al.*, *Trans. Amer. Clin. Climatol. Assoc.* **88**, 128 (1977). Crofford, *et al.* also discloses the use of head space analysis to determine the ketone concentration of liquid samples.

Current methods for the measurement of breath acetone levels include the use of gas chromatography. Rooth, *et al.*, *The Lancet*, 1102 (1966) discloses the use of a gas chromatograph capable of detecting acetone at concentrations of 2 to 4 nM of air with 18 nM being the concentration for breath of normal individuals. Subjects breathe directly into the device and the acetone peak is read after 40 seconds. Reichard, *et al.*, *J. Clin. Invest.* **63**, 619 (1979) discloses gas chromatographic techniques for the determination of breath acetone concentrations wherein breath samples are collected through the use of a calibrated suction flask into which the test subject breathes through a glass inlet tube. These methods and the instruments required for their use are complicated and expensive and tend to be impractical for use by consumers.

Other methods for the measurement of breath acetone levels involve the use of mass spectrographic equipment. Krotosynski, *J. Chrom. Sci.*, **15**, 239 (1977) discloses the use of mass spectrographic equipment in evaluating the ketone content of alveolar air. Twelve ketone components of breath were identified with acetone comprising the major component. Mass spectrographic methods suffer from the same limitations, however, as relate to gas chromatographic techniques.

Methods utilizing color reactions for the detection of acetone in liquid or air have also been

reported in the art. Greenberg, *et al.*, *J. Biol. Chem.* Vol. 154-155, 177 (1944) discloses methods for the determination of acetone levels apart from those of other ketone bodies in solution. The methods involve reaction of acetone and other ketones with 2,4-dinitrophenylhydrazine, to form hydrazone products which may then be separated and isolated owing to differing solubilities.

Peden, *J. Lab. Clin. Med.* **63**,332 (1964) discloses improvements over the methods of Greenberg, *et al.* utilizing salicylaldehyde as a coloring reagent. According to this method,  $\beta$ -hydroxybutyric acid is converted to acetone by oxidation with the amount of acetone formed measured by reaction with salicylaldehyde. Preformed acetone and acetoacetic acid are removed prior to the conversion of the  $\beta$ -hydroxybutyric acid by heating in the presence of acid. While these methods are useful for the determination of acetone concentrations apart from those of other ketone bodies they are complex and time consuming.

These various colorimetric methods known for detection of acetone in biological fluids are complex, time consuming and necessitate the use of a spectrophotometer or color charts. Moreover, the methods often require the use of high concentrations of alkali or acids. Alternative methods for the detection of acetone often require the use of complex and expensive apparatus. There thus continues to exist a need for devices for the quantitative determination of fluid acetone concentrations which are simple, accurate, inexpensive and do not require the use of high concentrations of hazardous reagents.

There exists a desire for devices for the measurement of the rate of fat catabolism. It is a particular problem that many individuals undergoing diets are unable to determine their rate of fat-loss because of daily variation in their body fluid content. Significantly, it is known that early in a diet individuals lose high proportions of fluid as compared to fat. Later in their diets, when individuals may still be catabolizing fat at a constant rate they may cease to lose fluids at the previous high rate or may, if only temporarily, regain fluid weight. The experience of hitting a plateau in weight loss or even regaining weight is psychologically damaging and weakens the subject's resolve to continue with the diet often with the effect that the subject discontinues the diet.

Recently, a method has been disclosed for the determination of daily rate of fat loss. Wynn, *et al.*, *Lancet*, 482 (1985) discloses that daily fat-loss may be calculated by subtracting daily fluid and protein mass changes from daily weight changes. Changes in body water are estimated from the sum of external sodium and potassium balances and protein mass changes are calculated from nitrogen bal-

ances. Such a method is complex and time consuming thus making it inconvenient for the consumer.

One set of methods for measuring body fat is by quantitating total body water (TBW). A number of methods are available for determining TBW. These include isotopic dilution procedures using deuteriated water, tritiated water and  $^{18}\text{O}$ -labelled water. Urine, blood serum or saliva samples are collected after a 2 to 4 hour equilibration. The fluid samples are then vacuum sublimed and the concentration of tracer in the sublimate is determined by mass spectrometer, gas chromatography, or infrared or nuclear magnetic resonance spectroscopy. Body composition can also be measured by a bioelectrical impedance method using a body composition analyzer. These methods are well known in the literature and are readily performed by those of skill in the art. Equipment for performing such measurements is available commercially from medical instrument manufacturers such as RJL Systems, Inc. (Detroit, MI).

Hydrostatic weighing method is a well known method wherein the subject is completely submerged in a tank of water and the body fat is calculated by taking into account the average density of fat and the amount of water displaced. This method is inconvenient and is still not completely accurate because assumptions must be made relating to nonfat density, lung capacity and other factors. Another method for calculating the percentage of body fat utilizes skin calipers to measure the thickness of fat deposited directly beneath the skin. Pincers are used to measure the thickness of folds of skin and fat at various locations on the body. The results of these measurements are compared with standardized tables to arrive at a figure for percentage of body fat. This method, while more convenient than the use of hydrostatic weighing is less accurate. All methods for determination of body fat content suffer from the fact that they do not reveal the rate of fat loss but only the fat content of the body at a particular time. Because means for determining body fat content are of limited accuracy, means for the determination of the rate of fat loss are similarly limited. Nevertheless it is desired that a simple and convenient device be developed for the determination of the rate of fat-loss wherein such a device is used as part of a method which is capable of distinguishing weight loss due to loss of fat as opposed to weight loss from the elimination of bodily fluids.

Of interest to the present invention are observations that ketosis occurs in non-diabetic individuals undergoing weight loss through diet, fasting or exercise. Freund, *Metabolism* **14**, 985-990 (1965) observes that breath acetone concentration increases on "fasting." It is disclosed that breath

acetone concentrations increased gradually from the end of the first day of the fast to approximately 50 hours into the fast at which time the concentration rose sharply in a linear fashion and reached a plateau on the fourth day. The acetone concentration of the plateau was approximately 300  $\mu\text{g/liter}$  (5,000 nM) a hundred-fold increase over the normal value of 3  $\mu\text{g/liter}$  (50 nM). When, instead of fasting, the subject was placed on a "ketogenic" diet with a minimum of 92% of calories derived from fat, the subject suffered a lesser degree of ketosis wherein the plateau had an acetone concentration of approximately 150  $\mu\text{g/liter}$  (2,500 nM).

Rooth, *et al.*, *The Lancet*, 1102-1105 (1966) discloses studies relating to the breath acetone concentrations of a number of obese and diabetic subjects. When the caloric intake of three non-diabetic obese subjects was reduced, their breath acetone concentrations as measured by a gas chromatograph increased approximately three-fold. On fasting, the subjects' breath acetone concentrations increased to one hundred times normal. Within 16 hours after a heavy meal the subjects' breath acetone concentrations dropped almost to normal. In a study of obese diabetic patients, the authors disclosed evidence that those obese patients who had lost weight in the last three months had higher breath acetone concentrations than those patients who had gained weight.

Walther, *et al.*, *Acta Biol. Med. Germ.* **22**, 117-121 (1969) discloses the results of a study on the effects of continued exercise of a well-trained cyclist. The authors disclose that breath acetone concentration, increases prior to, during and after the cessation of the physical load and reached a maximum 15 to 20 minutes after cessation of the physical load. Breath acetone concentrations approach a normal level one to two hours after the cessation of the physical load. It is suggested that the increased production of acetone is due to the increased utilization of plasma free fatty acids in liver and reduced utilization in peripheral tissue.

More recent studies have shown a correlation between fasting in normal and obese patients and increased blood acetone levels. Rooth, *et al.*, *Acta Med. Scand.* **187**, 455-463 (1970); Goschke, *et al.*, *Res. Exp. Med.* **165**, 233-244 (1975); and Reichard *et al.*, *J. Clin. Invest.* **63**, 619-626 (1979) all show the development of ketosis in both overweight and normal individuals during fasting. Rooth, *et al.*, (1970) suggests the use of breath ketone measurements as a motivational tool to enforce against dietary cheating. The studies disclose that development of ketosis is slower in overweight than in normal weight individuals. Reichard, *et al.*, discloses that there is a better correlation between breath acetone and plasma ketone concentrations than between urine ketone and plasma ketone con-

centrations. In addition, Rooth, *et al.*, (1970) discloses that certain urine ketone tests which detect the presence of acetoacetic acid are not entirely reliable because some individuals do not excrete acetoacetic acid in the urine despite increased blood serum concentrations.

Crofford, *et al.*, (1977) discloses the use of breath acetone monitoring for monitoring of diabetic conditions and as a motivational tool in following patients on long-term weight reduction programs. Such monitoring is said to be particularly effective as normalization of the breath acetone is disclosed to occur upon significant dietary indiscretion. Patients' breath samples were monitored using a gas chromatograph and it is suggested that patients be instructed to restrict their caloric input to that which will maintain breath acetone concentrations of approximately 500 nM. It is further suggested that if breath acetone is controlled at this level and the proper balance of carbohydrate, protein and fat are maintained in the diet that weight loss will occur at a rate of approximately one-quarter kilogram (one-half pound) per week.

#### SUMMARY OF THE INVENTION

The present invention relates to devices, kits and disposable columns for use in such kits for monitoring levels of various components in the breath of a user. The devices, kits and disposable columns of the invention contain material reactive to the presence of said breath components. The devices, kits and disposable columns of the invention may be useful, for example, in the quantitative determination of ketone and aldehyde, in particular acetone, concentrations for the purpose of monitoring the effects of diet, exercise and diabetic conditions.

The measurement of breath acetone utilizing the device, kit and analyzer column of this invention is also adoptable for monitoring the insulin dose requirement of Type 1 insulin-dependent diabetic patients and to distinguish between Type 1 (ketotic) and Type 2 (non-ketotic) diabetic patients.

The device, kit and analyzer column of the invention can be used for ascertaining the fat catabolism effects of a weight loss dietary regimen comprising diet, fasting or exercise through the quantitative determination of alveolar air (breath) acetone concentrations.

The device of the invention generally comprises a) an outer tubular member having an open first end and a second end; b) valve means disposed toward the second end of said outer tubular member; c) a breath sample collection means having one end mounted on said tubular member and having the other end closed, and having an interior in communication with the inside of said outer

tubular member through said valve means; and d) a disposable tubular analyzer column having a mouthpiece and containing material reactive to the presence of said breath components, wherein said column is insertable into said outer tubular member and cooperates with said valve means to permit breath blown by a user to pass through the outer tubular member into said sample collection means and to permit said collected breath sample to discharge through the reactive material of said analyzer column.

The kit of the invention generally comprises a) a portable housing adapted to receive a disposable analyzer column containing a mouthpiece and reactive materials; b) bag means in communication with said housing for collecting a fixed volume of a user's breath blown through the mouthpiece and discharging it at a substantially constant rate through the reactive materials; and c) valve means disposed in said housing which, in a first position, prevents such fixed volume of breath from contacting said reactive materials and, in a second position, permits contact of said breath with said reactive materials, said valve means being operable by insertion of the column into the housing.

The disposable tubular analyzer column for use in the kit of the invention generally comprises a hollow mouthpiece portion of a diameter permitting partial insertion of said analyzer column into a blow tube of said kit; a central portion of reduced diameter having an inclined wall segment interconnecting said mouthpiece and said reduced-diameter central portions, said central portion housing a volume of reactive material, and said inclined wall segment defining at least one breath passage opening connecting the hollow interior of the mouthpiece with the exterior of the central portion.

When the device, kit and analyzer column of the invention are used for the quantitative determination of serum acetone concentrations through the measurement of breath acetone concentrations, the material reactive to acetone preferably comprises a first solid matrix material to which a nitroprusside salt is coupled and a second solid matrix material to which a primary or secondary amine is covalently coupled. Preferably, the first and second solid matrix materials are in the form of discrete particles which are treated accordingly with a nitroprusside salt or an amine and are intermixed so as to place nitroprusside and amine moieties in intimate contact with one another. The solid matrix materials may be selected from a variety of materials including cellulose and silica gel which present suitable coupling moieties or are susceptible to reaction with suitable coupling moieties.

In the preferred method of measuring ketone and aldehyde concentrations, ketone or aldehyde

analytes present in a sample are contacted in the presence of a solvent with a nitroprusside salt coupled to a first solid matrix material and an amine covalently bound to a second solid matrix material. These materials together react to form detectable reaction products of characteristic colors which may then be observed for a qualitative or quantitative determination of the presence of ketone or aldehyde analytes.

The device of the invention may contain an adsorbant for preconcentration of the analytes wherein the adsorbant may be a material such as Tenax TA (a 2, 6-diphenyl-p-phenylene oxide polymer) or activated silica which may be maintained in the device in a preadsorbant zone separate from the first and second solid matrix materials associated with the nitroprusside salt and amine which are located in a reaction zone. After preconcentration, the ketone or aldehyde analytes are desorbed from the adsorbant by means of a solvent and contacted with the first and second solid matrix materials for reaction with the nitroprusside and amine reagents. According to a preferred embodiment, ketone and aldehyde components present in a vapor sample may be preconcentrated on the first and second solid matrix materials themselves. The analytes may then be solubilized by addition of a solvent to react with the nitroprusside and amine moieties present on the solid matrix materials. Where the analyte of interest is acetone methods for the assay of vapor samples, particularly breath samples, preferably utilize a desiccating bed for the preadsorption of water which can interfere with the quantitative detection of acetone.

In vapor sample devices wherein ketones and aldehydes are preconcentrated by adsorption onto the first and second solid matrix materials, a "linear reading system" for determination of analyte concentration may be utilized. The system provides a visual indication, in the form of a color bar of colored reaction products, indicating the quantity of ketone or aldehyde analytes adsorbed onto the first and second solid matrix materials. Because the adsorption sites on the matrix materials are limited, the extent to which ketone and aldehyde analytes will be adsorbed is dependent upon the quantity of analytes in the vapor sample. Analyte vapors will initially be adsorbed onto the solid matrix materials at the first portion of the reaction zone. As adsorption sites on those materials are saturated analyte vapors are adsorbed at more distant points within the reaction zone. Where the volume of the vapor sample is fixed, the distance from the first end of the reaction zone at which the analyte vapors are finally adsorbed is dependent upon the concentration of the analytes in the vapor sample. The extent to which the analytes are adsorbed, and hence the ketone or aldehyde concentration of the sample, is

indicated by the extent of formation of colored reaction products.

The device of the present invention utilizes a breath collection device into which a subject breathes and which can collect a selected amount of alveolar air. When the device is used for measuring breath acetone concentrations, the breath sample is then passed through the analyzer device wherein an anhydrous calcium chloride desiccant bed removes water vapor from the breath sample. The sample is then passed through a bed filled with a mixture of first and second solid matrix materials comprising nitroprusside-DEAE silica gel and aminopropyl silica gel where acetone contained within the breath is adsorbed into the matrix. The distance to which the acetone is adsorbed is dependent upon the total amount of acetone present in the sample. A solvent mixture containing either methanol or methanol and dimethyl sulfoxide (DMSO) is then added to the matrix to activate the color reaction and form a blue color bar. The length of the color bar is proportional to the concentration of acetone in the fixed breath sample volume and may be compared with a table or calibration marks on the side of the matrix bed to determine the breath and serum acetone concentrations.

The devices of the present invention may be utilized to monitor diabetic patients, to analyze for various metabolic abnormalities or may be utilized according to one aspect of the present invention for the monitoring of the rate of fat catabolism. It has been found that serum acetone concentrations and hence breath acetone concentrations which can be measured by the devices of the present invention may be correlated directly with the rate of fat catabolism and fat-loss experienced by a subject undergoing a weight loss dietary regimen comprising fasting, dieting, exercise or a combination of the three. Serum and breath acetone concentrations may be determined and the rate of fat-loss calculated therefrom. The devices of the invention are extremely convenient, are accurate within about 10% in determining serum acetone levels and are therefore particularly suitable for measuring fat catabolism and the rate of actual fat-loss as opposed to determining weight loss which is variable and often reflects variations in fluid losses. By measurement of breath acetone levels, a subject will be able to estimate with a high degree of accuracy his rate of fat-loss, the water-loss/fat-loss ratio and be able to adjust his diet and amount of exercise according to his desired weight loss goals.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a view of a vapor test device of the present invention.

FIG. 2 is a view of an alternative vapor test device of the present invention.

FIG. 3 is a perspective view of a breath-sampling kit of the present invention.

FIG. 4 is an exploded perspective view of the kit shown in FIG. 3.

FIG. 5 is an exploded perspective view of the outer tubular member of blow tube of the kit shown in FIGS. 3 and 4.

FIG. 6 is an enlarged fragmentary longitudinal sectional view taken generally along line 25-25 of FIG. 5.

FIG. 7 is a perspective view of a disposable analyzer column which is usable with the breath-sampling kit of FIGS. 3 and 4.

FIG. 8 is a side elevational view of the breath-sampling assembly of the present invention with the housing portions of the kit removed and showing the position of the parts and the flow of air when a user is blowing into the mouth piece to expand the inflatable bag and provide a known-volume of breath to be analyzed.

FIG. 9 is an end elevational view, partially in transverse section, of the assembly taken generally along the line 28-28 of FIG. 8.

FIG. 10 is a side elevational view of the assembly of FIG. 8 showing the position of the parts and the flow of air when the collected sample of air is being discharged from the bag through the analyzer column.

FIG. 11 is an end elevational view, partially in transverse section, of the assembly taken generally along the line 30-30 of FIG. 10.

FIG. 12 is a transverse sectional view taken generally along line 31-31 of FIG. 10.

FIG. 13 is a fragmentary longitudinal sectional view taken generally along line 32-32 of FIG. 10 showing the unbroken ampule of reactant in the disposable analyzer column.

FIG. 14 is a fragmentary longitudinal sectional view similar to FIG. 13 but showing the ampule of reactant after same has been broken.

FIG. 15 is a transverse sectional view taken generally along line 34-34 of FIG. 8 with the analyzer column in its first rotary and axial position (breath-receiving mode) in the blow tube.

FIG. 16 is a transverse sectional view taken generally along line 35-35 of FIG. 10 with the analyzer column in its second rotary and axial position (breath-discharging mode) in the blow tube.

FIG. 17 is a transverse sectional view taken generally along line 36-36 of FIG. 8.

FIG. 18 is an enlarged fragmentary longitudinal sectional view showing the valve operation of the breath-sampling assembly when a user is blowing into the mouth piece as shown in FIG. 8.

FIG. 19 is an enlarged fragmentary longitudinal sectional view similar to FIG. 18 that is showing the valve operation after the user has completely filled the breath collection bag, a static condition during which the breath sample is retained in the collection bag.

FIG. 20 is an enlarged fragmentary longitudinal sectional view similar to FIGS. 18 and 19 but showing the valve operation after the analyzer column has been rotated 90 degrees from its initial position and then pushed further inwardly into the blow tube to the position shown in FIGS. 10 and 20 whereby the collected sample of breath is forced through the analyzer column and out through the mouth piece as a result of biased deflation of the collection bag.

#### DETAILED DESCRIPTION

The present invention comprises devices, kits and disposable columns for use in such kits for monitoring levels of various components in the breath of a user. The breath-testing devices and analyzer columns will be first generally discussed with reference to Figures 1 and 2. Particular embodiments of the breath-testing devices of the present invention will then be discussed in more detail with reference to Figures 3-20.

#### VAPOR TEST DEVICES

The devices of the present invention are suitable for the detection of ketone and aldehyde analytes in gaseous (vapor) forms. Vapors which may be analyzed for the presence of such analytes include atmospheric air, laboratory and industrial vapors, breath and other vapors for which the quantitative analysis of ketone or aldehyde content is desired. A particular aspect of the present invention comprises devices for the quantitative detection of acetone in human breath. Such detection is useful for the monitoring of serum acetone levels which is of value to diabetics in monitoring the onset of ketosis. Such detection is also useful to the quantitative monitoring of fat catabolism.

Referring to the drawing, Figure 1 depicts a vapor test device (10) for the detection of ketone or aldehyde analytes present in a vapor sample comprising a length of inert cylinder (11) having a first end (12) at which a vapor sample may be introduced to the device by a sample means and a second end (13) at which vapor is exhausted from the device. Within the inert cylinder (11) and progressing from the first end (12) to the second end (13) are a first porous barrier (14), a second porous barrier (15), a third porous barrier (16) and a fourth porous barrier (17). The first porous barrier (14) and the second porous barrier (15) define a

pretreatment zone (18) filled with desiccant means. The second (15) and third (16) porous barriers define a reaction zone (19) filled with, for example, a first solid matrix material to which a nitroprusside salt is coupled and a second solid matrix material to which an amine is covalently bound. The reaction zone (19) may also comprise an axially aligned filler rod (22) which fills space within the reaction zone (19) and increases the length of the device over which a fixed volume of the first and second solid matrix materials are spread. Said third porous barrier (16) and said fourth porous barrier (17) define a solvent zone (20) in which is located a solvent ampule (21).

According to a procedure for use of the device, a fixed volume of sample vapor is introduced to the first end (12) of the device by suitable sample means and is allowed to flow through the length of the device before it is exhausted from the second end (13). As sample vapor flows through the device, water vapor present in the sample is adsorbed by desiccant means present in the pretreatment zone (18). Dehydrated vapor then flows through the reaction zone (19) where ketones and aldehydes present in the vapor are adsorbed by the first and second solid matrix materials. Analytes are first adsorbed at the end of the reaction zone (19) adjacent to the first porous barrier (14) closest the first end (12) but as the volume of vapor sample is passed through the device the solid matrix materials closest the first end become saturated and additional analytes are adsorbed onto the solid matrix materials progressively farther from the first end (12). Where the volume of the sample is fixed the distance to which the analytes are adsorbed into the reaction zone (19) may be directly correlated with the concentration of analytes present in the sample.

When the volume of sample vapor has been passed through the device, the solvent ampule (21) is broken allowing a volume of solvent to pass downward through the third porous barrier (16) into the reaction zone (19) where the first and second solid matrix materials are thoroughly wetted with the solvent. If a nitroprusside salt has been coupled to the first solid matrix material and an amine has been covalently bound to the second solid matrix material then they will react in the presence of solvent with ketones and aldehydes adsorbed onto the solid matrix materials to form colored reaction products which form a colored bar in the device. These reaction products provide a visual signal indicating the areas of the reaction zone where vapor ketones were adsorbed and thus the concentration of analytes present in the sample.

Referring to the drawing, Figure 2 depicts an alternative vapor test device (30) for the detection of, for example, ketones and aldehydes in a vapor

sample comprising a length of inert cylinder (31) having a first end (32) at which a vapor sample may be introduced and a second end (33) at which vapor is exhausted from the device. Within the inert cylinder (31) and progressing from the first end (32) to the second end (33) are a first porous barrier (34), a second porous barrier (35) and a third porous barrier (36). The first porous barrier (34) and the second porous barrier (35) define a preadsorbant zone (37) which is filled with an adsorbant material capable of selectively adsorbing ketone and aldehyde analytes. The second porous barrier (35) and third porous barrier (36) define a reaction zone (38) filled with, for example, a first solid matrix material to which a nitroprusside salt is coupled and a second solid matrix material to which an amine is covalently bound.

According to a procedure for use of the device, a fixed volume of sample vapor is introduced to the first end (32) of the device by suitable sample means and is allowed to flow through the length of the device before it is exhausted from the second end (33). Ketones and aldehydes present in the sample vapor are selectively adsorbed on the adsorbant material present in the preadsorbant zone (37). When the volume of sample vapor has been passed through the device a quantity of solvent is introduced to the first end (32) of the device which then desorbs analytes adsorbed in the preadsorbant zone (37) and transports them to the reaction zone (38). There the analytes react in the presence of the solvent with, for example, nitroprusside salts coupled to a first solid matrix material and an amine covalently bound to a second solid matrix material to form a colored reaction product.

#### Analyzer Column

The analyzer column comprises an inert cylinder fabricated from a material which will neither react with nor adsorb ketones or aldehydes and which is nonreactive with the reagents utilized in the assay. The column materials are preferably transparent in order that the presence of a color reaction product may be detected and evaluated. Preferred materials include transparent plastics such as polystyrene and polyethylene terephthalate. Glass tubes are acceptable but columns fabricated from polyethylene terephthalate are particularly preferred. Where the device is one according to Figure 1, the cylinder is preferably somewhat flexible in order that pressure may be applied to rupture the solvent ampule. Alternatively, where the solvent ampule comprises a readily puncturable end such as one of metal foil, means such as a plunger means may be incorporated with the device to free solvent from the ampule. The analyzer column may be of generally any size and geometry



selected to contain sufficient reagents to analyze a sample of a selected size. According to one embodiment the column comprises a polyethylene terephthalate cylinder 13 cm long with an inner diameter of 0.8 cm. The cylinder is divided by means of three 0.5 cm porous barriers defining pretreatment zone 1.3 cm long, a reaction zone, 3.0 cm long and a 4.0 cm long solvent zone containing a solvent ampule. Optionally present in the reaction zone is filler means which may be an axially centered rod which can be used to fill a portion of the volume of the reaction zone and thereby elongate the length of the zone filled by a fixed volume of the first and second solid matrix materials. The rod itself may be transparent or opaque and should be inert to the analytes and reagents of the invention. It is preferably fabricated from polystyrene, being polyethylene terephthalate, or polypropylene with polypropylene being particularly preferred.

#### Porous Barriers

Porous barrier materials suitable for use with devices of the present invention include those materials which are inert to and nonreactive with the analytes and reagents of the invention and are porous with respect to the passage of vapor samples and solvents utilized in such devices. Suitable materials include various porous materials such as nylon fabric, glass wool, sponge, styrofoam and other ceramic and plastic materials. Preferred materials for use with the vapor phase devices of the present invention are porous polyethylene frits with a pore size of 100  $\mu\text{m}$  (Porex Technologies, Fairburn, GA).

#### Preadsorbant Materials

Preadsorbant materials suitable for use with the present invention include those materials which are capable of selectively adsorbing ketone and aldehyde analytes from vapor samples. Such materials should also readily and completely desorb such analytes in the presence of preferred solvents of the invention such as methanol and methanol with dimethylsulfoxide (DMSO). Suitable materials include activated silica gel. A particularly preferred material is Tenax TA (a trademark of Enka N.V., Arnhem, Netherlands) a 2,6-diphenyl-p-phenylene oxide polymer.

#### Desiccant Means

Vapor analyzer devices according to the present invention which are designed for the analysis of vapors containing water vapor, particularly breath, require means for the removal of water

from the vapor sample prior to reaction with the assay matrix. This is particularly so where the material analyzed for is acetone, as the presence of water substantially reduces the rate of reaction of acetone with the nitroprusside and amine reagents of the invention. While a variety of desiccant materials are available which are capable of pre-drying vapor samples, it is desired to utilize a material which is inexpensive, safe and will not adsorb or react adversely with the ketone or aldehyde components of the vapor samples. Materials such as granular silica, anhydrous calcium sulfate, molecular sieve type 3A or 4A (W.R. Grace, Baltimore, MD), magnesium perchlorate, activated charcoal, Bio-beads SM-2 and SM-4 (styrene-divinyl copolymers obtained from Bio-Rad Laboratories, Richmond, CA) are generally undesirable materials because of their tendency to adsorb acetone. Ascarite II (841-1000  $\mu\text{m}$  particle size (16-20 mesh)) (obtained from Thomas Scientific, Swedesboro, NJ) is an excellent desiccant and does not adsorb acetone but comprises sodium hydroxide silica particles and is corrosive and unsuitable from a handling standpoint.

A preferred material is anhydrous calcium chloride in pellet form. Various commercially available materials are suitable, although a particularly preferred material may be obtained in pellet form from Dow Chemicals, Ludington, Michigan as type 94 XFS 43284. The material may be fractured using a Fritzmill size reduction instrument (Fritzpatrik Company, Elmhurst, IL) and sized to between 707 and 1000  $\mu\text{m}$  (16 and 24 mesh). The preferred calcium chloride granules are then heated at 200°C for 20 hours and are stored in a closed bottle. The amount of moisture permitted for the preferred calcium chloride is between 0-0.5%. The amount of calcium chloride needed for removal of moisture from vapor samples may readily be determined by one of skill in the art. The amount of calcium chloride required for removal of moisture from a 450  $\text{cm}^3$  breath sample is between 120 and 180 mg.

It has been established that 150 mg of calcium chloride (Dow 94 XFS, 707-1000  $\mu\text{m}$  particle size (16-24 mesh), 0-0.4% moisture) adsorbs 100% of moisture from a 450  $\text{cm}^3$  breath sample. The amount of moisture in a 450  $\text{cm}^3$  breath sample is  $4.90 \pm 0.99$  (SD,  $n = 56$ ). The recovery of acetone vapor from 450  $\text{cm}^3$  breath samples ( $n = 20$ ) using same amount of calcium chloride is also 100%. It is important to note that if the amount of anhydrous calcium chloride exceeds about 200 mg, there is a tendency to adsorb acetone from 450  $\text{cm}^3$  breath samples. Other types of calcium chloride such as Type P 90 (Dow Chemical) obtained in pellet form and fractured to the desired 707-1000  $\mu\text{m}$  particle size (16-24 mesh

size) can also be used to remove moisture from breath and other vapor samples. To reduce the moisture content of P 90 calcium chloride to less than 0.5%, it must be heated at 200 °C for at least 48 hours. The material may then be stored in a closed container until needed.

### Sample Means

The devices of the present invention for the quantitative detection of ketones and aldehydes in vapor samples require means for the introduction of a fixed quantity of vapor sample to the detection column. Suitable means are those which comprise materials which are inert with respect to the ketone samples and are capable of reproducibly delivering a fixed volume of sample vapor to the device. It is desired that vapor samples be introduced to the devices of the invention at a relatively steady rate in order that analytes present in the sample be reproducibly adsorbed on the first and second solid matrix materials of the reaction zone. Unsteady vapor flow into the devices may cause analytes to be unevenly adsorbed onto the matrix materials of the device with the consequence that inconsistent and unreproducible analyte concentrations would be indicated by the assay devices.

Balloons and bags are particularly suitable for such applications although it is necessary that the material from which the bag or balloon is constructed be inert to the ketone and aldehyde materials of the sample. It was found that rubberized films and polyvinyl films adsorbed greater than 25% of acetone present in a breath sample in ten minutes. Films found to be suitable included those fashioned from nylon, teflon, very low density polyethylene, and a copolymer of polyester with polyvinyl chloride/vinylidene chloride (Saran). Bolton, *et al.*, U.S. Patent No. 4,579,826 herein incorporated by reference, describes methods and devices for sampling of predominantly alveolar breath. Bolton, *et al.* specifically discloses one device comprising a non-self-supporting polymeric tube and a spring means effective to roll the tube upon itself in spiral fashion toward the mouthpiece unit.

Particularly preferred due to high permeability of water vapor and its durability and low cost is the use of bags of 25  $\mu$ m (1 mil) thick nylon. According to one embodiment, a nylon bag with a capacity of 450 cubic centimeters is attached to a valve device comprising a column, a mouthpiece, and a plunger. With the plunger set in one position the test subject takes a deep breath, holds it for five seconds and blows a breath sample into the device at a steady rate until the sample bag is completely inflated. The plunger is then pushed down to an

alternate position and the sample bag is steadily deflated by a spring means blowing the sample vapor through the device and contacting analytes with either the preadsorbent bed or the nitroprusside and amine treated first and second matrix materials. Where the material to be sampled is atmospheric air or an industrial or laboratory vapor sample, a sample port may be substituted for the mouthpiece. Vapor samples may be collected by a bellows or other suitable means and appropriate volumes of material introduced to the device.

With reference now to Figures 3-20 one embodiment of a breath-sampling kit for practicing a method of the present invention will now be described. As best illustrated in Figures 3, 4 and 7, a breath-sampling kit (50) includes a portable housing (52) characterized by: an elongated base (54) having an inverted U-shaped portion (56) open at its right end (as viewed in Figure 4) and having an integral depending but upwardly opening U-shaped portion (58) at its left end, defining a vertically disposed compartment (60) open at its right end but including an end wall (62) at its left end having a circular opening (64) provided therein; a breath-sampling assembly (66) which is fitted in the base (54) and retained therein by a cover (68) which is characterized by an elongated U-shaped portion (70) having a vertically disposed end wall (72) at its left end (as viewed in Figure 4) which is adapted to overlay the end wall (62) of the base (54); and an end cap (74) which fits over and closes the right end of the housing (52) in a suitable manner. The meeting edges (76) and (78) of the U-shaped portions (56) and (70) of the base (54) and the cover (68), respectively, are designed for interfitting engagement in a known manner. The kit (50) also includes a breaker button (80) which is disposed in an opening (82) provided in a side wall of the housing base (54) for a purpose which will be described in detail hereinafter. A slightly raised marker (84) depends from the bottom of an opening (64) on the outer surface of the end wall (62) of the compartment (60) for a purpose which will also be described hereinafter.

As best illustrated in Figures 4, 5, 8 and 9, the breath-sampling assembly (66) is characterized by: an elongated outer tubular member or blow tube (86) which is formed of a transparent inert plastic material and which has an opening (88) formed in the side wall thereof toward the bottom of the tube (86); an inflatable/deflatable air or breath collecting plastic bag (90) having a specific volumetric capacity and having an open end secured to the outer surface of the tube (86) and in communication with the opening (88) provided therein, the opposite end of the bag (90) being closed and secured to a rigid support member (92) which is disposed generally parallel to the tube (86); a valve housing (94) which

is secured in a valve housing recess (96) provided in the lower end of the tube (86); a ball valve (97) which may be formed of polypropylene and which is disposed in an axial recess (98) provided in the inner end of the valve housing (94) and; an O-ring (100) which is retained against downwardly facing O-ring seating means (102) provided in the tube (86) by the inner end of the valve housing (94). As best illustrated in Figures 18, 19 and 20, the inner end of the valve housing (94), which is reduced in diameter relative to the outer end, is provided with a diametrically extending bore (104) which is axially aligned with tee opening (88) in the blow tube (86) to the bag (90) and with a pair of diametrically opposite vertically extending slots (106) adjacent to but spaced from the inner end of the valve housing (94) with a lower valve seat (108) for the ball valve (97) being defined in the recess (98) above the lower end of the slots (106) for a reason which will be made clear hereinafter. It is also noted that the diameter of the ball valve (97) is somewhat greater than the inner diameter of the O-ring (100).

With reference to Figures 5, 6, 16, 17, 18, 19 and 20, it is noted that the inner surface of the blow tube (86) is provided with four equidistantly spaced, longitudinally extending ribs (110) and (112). Three of the ribs (110) terminate short of the upper end of the blow tube (86) by a distance approximately equal to 1/5 of the overall length of the tube (86). The fourth rib (112) terminates almost at the upper end of the tube (86). All four of the ribs (110) and (112) converge inwardly at their lower ends to define the O-ring seating means (102). As shown in Figure 6, the upper end of the rib (112) is provided with a stepped configuration to define a first holding surface (114) for the analyzer column and a second positive stop surface (116). An external annular rib (118) at the upper end of the tube (86) limits insertion of the blow tube (86) into the opening (64) provided in the end wall (52) of the housing compartment (60). The blow tube (86) is also provided with a button hole (120) which is adapted to be radially aligned with the breaker button opening (82) in the housing base (54) when the breath-sampling assembly (66) is fitted in the housing base (54).

A disposable analyzer column (122) is provided for use with the breath-sampling assembly (66) described herein. As best illustrated in Figures 7, 8, 10 and 13-20 the disposable analyzer column (122), which is formed of a transparent inert plastic having a degree of flexibility as previously noted herein, is characterized by a tubular member (124) having a series of axially spaced zones which will be defined hereinafter. The tubular member (124) has an upper mouth piece portion (126) of a diameter which is receivable in the open end of the blow tube (86) seated in the opening (64) in the

housing base (54), which opening is exposed upon the removal of the cover (68). The tubular member also has a first reduced-diameter portion (128), which comprises a major portion of the length of a column (122), and a second further reduced-diameter end portion (130) of a relatively short length. An annular shoulder (132) is defined between the two reduced-diameter portions (128) and (130) and an inclined or frusto-conical wall segment (134) is defined between the mouth piece portion (126) and the first reduced-diameter portion (128). For a purpose which will be discussed hereinafter, a series of air or breath openings (136) are provided in the inclined wall segment (134). The openings (136) preferably are equidistantly, circumferentially spaced around the wall segment (134) as illustrated in Figure 15. Further, as illustrated in Figures 7, 8, 15 and 16, a pair of diametrically opposite longitudinally extending flats (138) are provided on the outer surface of the mouth piece portion (126), which flats (138) extend from the inclined wall segment (134) for a distance approximately equal to 1/2 of the length of the mouth piece portion (126), at which point inwardly facing shoulders (140) are defined.

Within the analyzer column (122), from the lower end to the upper end as viewed in Figure 7, there is provided a first porous barrier or frit filter (142) which is secured in the end of the second reduced-diameter end portion (130); a second porous barrier or frit filter (144) which is seated against the annular shoulder (132) defined between the two reduced-diameter portions (128) and (130); an inert filler rod (146) having a longitudinal slot (148) formed therein which is seated against the filter (144) in the first reduced-diameter portion (128); a third porous barrier or frit filter (150) which is seated against the opposite upper end of the filler rod (146); a breakable ampule (152) containing liquid solvent or reactant disposed in the first reduced-diameter portion (128) above the third filter (150); and a fourth porous barrier or frit filter (154) which is provided in the first reduced-diameter portion (128) above the ampule (152). Each of the porous filters or frits is held in place by friction or raised projections on the inner surface of the analyzer column (122).

With reference again to the axially spaced zones of the analyzer column (122), a pretreatment zone (156) is defined in the second reduced diameter end portion (130) between the first and second porous barriers or filters (142) and (143). The pretreatment zone (156) is filled with a suitable desiccant means (158) such as  $\text{CaCl}_2$ . A reaction zone (160) is defined between the second and third filters (144) and (150) in that the longitudinal slot (148) in the filler rod (146) is filled with one or more solid reactive materials (162) as described else-

where. A solvent zone (164) in which the ampule (152) is disposed is defined between the third and fourth filters (150) and (154). As previously noted, herein the filler rod (146) fills a substantial portion of the space within the reaction zone (160) and thus increases the length of the zone (160) over which a fixed volume of a solid reactive material or materials (162) is spread. As best shown in Figures 8, 10, 13 and 14, indicia markings (166) may be provided on the filler rod (146) adjacent to slot (148).

Before describing how the breath-sampling kit (50) is used to collect and test a sample of a person's breath, reference is first made to Figures 3, 4, 5 and 12 showing the breaker button (80), and to Figures 13 and 14. The breaker button (80) is characterized by: a manually depressable head portion (168) which is freely receivable in the opening (82) provided in the housing base (54); an inwardly projecting stem portion (170) which extends through the opening (120) provided in the blow tube (86) and which is retained therein by an enlarged head (172) on the end thereof; and a coil spring (174) which is disposed about the stem portion (170) between the underside of the breaker button head (168) and the outer surface of the blow tube (86), whereby the breaker button (80) is normally biased away from the blow tube (86). As shown in the drawings, the breaker button (80) is longitudinally positioned on the blow tube (86) such that the stem head (172) is aligned with the solvent zone (164) of the analyzer column (122) when the analyzer column (122) is inserted into the blow tube (86) during a collection and testing procedure. Thus, sufficient inward pressure on the breaker button (80) forces the stem head (172) against the flexible solvent zone portion (164) of the analyzer column (122) with sufficient pressure to break the ampule (152) and permit the reactant solvent to flow downwardly through the "exposed" reactive material or materials (162) in the longitudinal slot (148) of the filler rod (146). Obviously, the ampule (152) should preferably be broken at the end most closely adjacent to the reaction zone (160) as shown in the drawings, to ensure a maximum flow of the reactant/solvent. If the ampule (152) were broken at an upper end, it is possible that part of the reactant/solvent would be retained in the unbroken lower portion of the ampule (152) with unreliable test results possibly resulting therefrom.

To collect and test a sample of a person's breath using the breath-sampling kit disclosed herein, the cover (68) is first removed from the portable housing (52) to provide access to the open end of the blow tube (86) and also to permit inflation of the collection bag (90). When one of the disposable analyzer columns (122) is first inserted into the blow tube (86), it is important that one of

the flats (138) on the mouth piece portion (126) be aligned with the raised marker (84) provided on the end wall (72) of the housing base (54). This ensures that neither of the flats (138) will be in initial alignment with the fourth rib (112) which, as can be seen in Figure 4 is positioned 90° from the raised marker (84). Therefore, the inclined wall segment (134) engages the second or positive stop surface (116) on the rib (112) to limit further inward movement of the analyzer column (122). In this rotational and axial position of the analyzer column (122), the breath-sampling assembly (66) is in its breath-collecting mode wherein the parts are positioned as shown in Figures 8, 9, 15 and 18. In this mode, as best illustrated by the arrows in Figures 8, 9 and 18, the person whose breath is to be tested or monitored blows into the mouth piece (126) with the blown breath passing through the mouth piece (126), through the air openings (136) in the inclined wall segment (134) and longitudinally through the space defined between the inner surface of the blow tube (86) and the outer surface of the first reduced-diameter portion (128) of the analyzer column (122). This is the path of least resistance due to the frit filters (154, 150, 144 and 142) disposed within the analyzer column (122). The blown breath proceeds through the O-ring (100) and into the recess (98) provided in the valve housing (94), through the slots (106) around the ball valve (97), through the aligned valve housing bore (104) and the blow tube opening (88) into the inflatable/deflatable collection bag (90). As illustrated in Figures 8 and 9, the bag (90) is fully inflated against the force of a flat coil spring (176) which is adhesively secured to the outer surface of the bag (90) approximately midway between the opposite side edges thereof to provide a known volume of a user's breath. The spring (176) normally biases the bag (90) into the deflated rolled-up condition as shown in Figure 4.

Once the bag (90) has been filled to its capacity, the user stops blowing and the bag (90) remains in its fully inflated condition inasmuch as the back pressure of the filled bag (90) forces the ball valve (97) into sealing engagement against the underside of the O-ring (100), as is clearly illustrated in the static mode of Figure 19.

To discharge the collected sample of breath or air past the reactive material (162), the analyzer column (122) is first rotated 90° (in either direction) to align one of the flats (138) with the longest rib (112) (see Figure 16) whereby the analyzer column (122) may now be advanced further into the blow tube (86) to its second rotational and axial position, best illustrated in Figures 10 and 20. In this deflation mode, the second reduced-diameter end portion (130) of the analyzer column (122) passes through and engages the O-ring (100) to

seal off the external passage of lesser resistance, as well as forcing the ball valve (97) downwardly against its lower valve seat (108). This action permits the bag (90) to deflate, at a substantially constant rate due to the spring (176) with the discharged air passing from the bag (90) through the blow tube opening (88), the aligned valve housing bore (104), the slots (106) around the seated ball valve (97), and finally through the first frit filter (142) into the analyzer column (122). It then passes through the pretreatment zone (156), the reactive zone (160), the solvent zone (164), and out through the mouth piece (126), since the lesser resistance passage is blocked. The ampule (152) may then be broken by applying inward pressure on the breaker button (80) as previously described herein.

It is noted that the ball check valve (97) described herein could be replaced by other known type valve arrangements such as a flapper valve. To provide for air flow through the analyzer column (122) in the bag deflation mode when a flapper valve is used, transverse notches are provided in the inner end of the analyzer column (122).

The testing procedure has been thoroughly discussed previously herein in connection with the testing device of Figure 1 and therefore will not be repeated herein.

After the breath-sampling test has been completed, the used analyzer column (122) is disposed of and a new analyzer column (122) can be used with the same kit (50) for a further test.

#### Solvents

For the detection of ketone and aldehyde analytes using nitroprusside and amine reagents, in the devices of the invention, suitable solvents must provide an environment in which ketone and aldehyde analytes may react with the nitroprusside and amine reagents. Where analytes are adsorbed onto preadsorbant materials suitable solvents must be capable of desorbing the analytes and transporting them to the reaction zone. Such solvent include methanol although a preferred solvent mixture comprises dimethyl sulfoxide (DMSO) and methanol at a 1:3 ratio by volume containing 30 mg/ml TRISMA-base. A particularly preferred solvent mixture is that comprising DMSO and methanol at a 1:3 ratio by volume containing 5 µl/ml N,N-diethanolamine (DEA).

As described above, such solvents are contained in the ampule (152) which may be broken to release the solvent.

Where technical features mentioned in any claim are followed by reference signs, those reference signs have been included for the sole purpose of increasing the intelligibility of the claims and accordingly such reference signs do not have

any limiting effect on the scope of each element identified by way of example by such reference signs.

#### 5 Claims

1. A device for monitoring levels of various components in the breath of a user, comprising:

- a) an outer tubular member (86) having an open first end and a second end;
- b) valve means (94, 97) disposed toward the second end of said outer tubular member;
- c) a breath sample collection means having one end mounted on said tubular member and having the other end closed, and having an interior in communication with the inside of said outer tubular member (86) through said valve means (94, 97); and
- d) a disposable tubular analyzer column (122) having a mouthpiece (126) and containing material reactive to the presence of said breath components, wherein said column (122) is insertable into said outer tubular member (86) and co-operates with said valve means (94, 97) to permit breath blown by a user to pass through the outer tubular member (86) into said sample collection means and to permit said collected breath sample to discharge through the reactive material of said analyzer column (122).

2. The monitoring device as recited in claim 1 wherein said analyzer column is insertable into said outer tubular member to a first rotational and axial position for breath collecting in which breath blown into the mouthpiece bypasses said reactive material and passes through said valve means into said collecting means, said analyzer column being rotatable and further insertable to a second rotational and axial position for breath sample discharging in which a collected breath sample is discharged through said valve means into said reactive material from said collecting means.

3. The monitoring device as recited in claim 1 wherein the analyzer column further comprises a reduced-diameter central portion creating a passageway between the inside of said outer tubular member and the outside of said analyzer column, said central portion being connected to said mouthpiece by an inclined wall segment having at least one orifice therein such that, when said valve means is in a first position, the breath of a user passes from said mouthpiece through said passageway to said sample collecting means.

4. The monitoring device as recited in claim 1 wherein longitudinally extending rib means are provided on the inner surface of said outer tubular member for guiding said analyzer column when inserted therein. 5
5. The monitoring device as recited in claim 4 wherein positioning flats are provided on said analyzer column for cooperation with said rib means on said outer tubular member. 10
6. The monitoring device as recited in claim 4 wherein stop means are provided on at least one of said rib means for engagement by said analyzer column to determine a first axial position of said column. 15
7. The monitoring device as recited in claim 2 wherein said valve means comprises a housing member, a ball member disposed therein, an O-ring, and a further reduced-diameter end portion of said analyzer column, said further reduced-diameter end portion of said column being axially spaced from said O-ring in said first position of the column and, in said second position of the column, passing through and sealingly engaging said O-ring and abutting against said ball. 20 25
8. The monitoring device as recited in claim 2 wherein said sample collection means comprises an inflatable/deflatable bag and a flat coil spring is provided on the outer surface of said bag so that, after said bag is inflated and said analyzer column is moved into said second position, said spring coils said bag into its deflated condition with the fixed volume of air being discharged at a substantially constant rate through said reactive material in the analyzer column. 30 35 40
9. The monitoring device as recited in claim 1 wherein said reactive material includes at least one fluid reactant, said tubular analyzer column has a flexible portion adjacent said reactive material and said outer tubular member includes means for squeezing said flexible portion thereby to break an ampule of said fluid reactant disposed in said flexible portion. 45
10. The monitoring device as recited in claim 9 wherein said means for squeezing comprises an outwardly biased but inwardly movable breaker button mounted in a portable housing surrounding said outer tubular member, said breaker button being in alignment with said flexible portion of the disposable analyzer column and having a stem and head for transferring pressure to said flexible portion. 50
11. The monitoring device as recited in claim 9 wherein said means for squeezing is axially positioned to break the end of said ampule most closely adjacent said reactive material. 55
12. A kit for the determination of levels of various components in a user's breath, said kit comprising:
  - a) a portable housing adapted to receive a disposable analyzer column containing a mouthpiece and reactive materials;
  - b) bag means in communication with said housing for collecting a fixed volume of a user's breath blown through the mouthpiece and discharging it at a substantially constant rate through the reactive materials; and
  - c) valve means disposed in said housing which, in a first position, prevents said fixed volume of breath from contacting said reactive materials and, in a second position, permits contact of said breath with said reactive materials, said valve means being operable by insertion of the column into the housing.
13. A disposable, tubular analyzer column for use in a kit for monitoring levels of various components in the breath of a user, said analyzer column comprising:
  - a hollow mouthpiece portion of a diameter permitting partial insertion of said analyzer column into a blow tube of said kit;
  - a central portion of reduced-diameter having an inclined wall segment interconnecting said mouthpiece and said reduced-diameter central portions, said central portion housing a volume of reactive material, and said inclined wall segment defining at least one breath passage opening connecting the hollow interior of the mouthpiece with the exterior of the central portion.
14. The analyzer column as recited in claim 13 wherein said central portion also houses a breakable ampule of liquid reactant adjacent said reactive material, said central portion being flexible enough to permit breaking of said ampule by applying pressure to said central portion.
15. The analyzer column as recited in claim 13 wherein said tubular member is further characterized by an end portion opposite said mouthpiece portion, said end portion having a further reduced-diameter which is operably engageable with valve means of said kit in at

least one position of said analyzer column in  
the blow tub of said kit.

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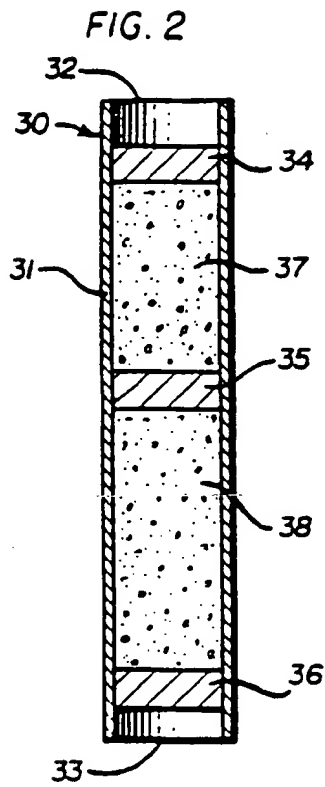
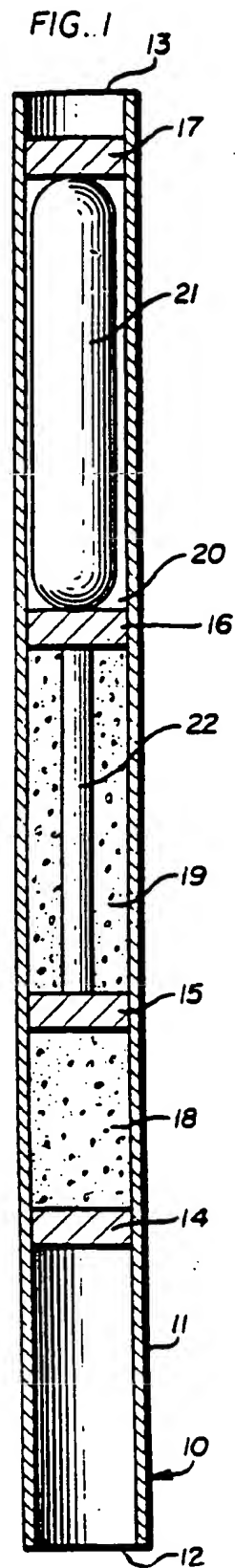
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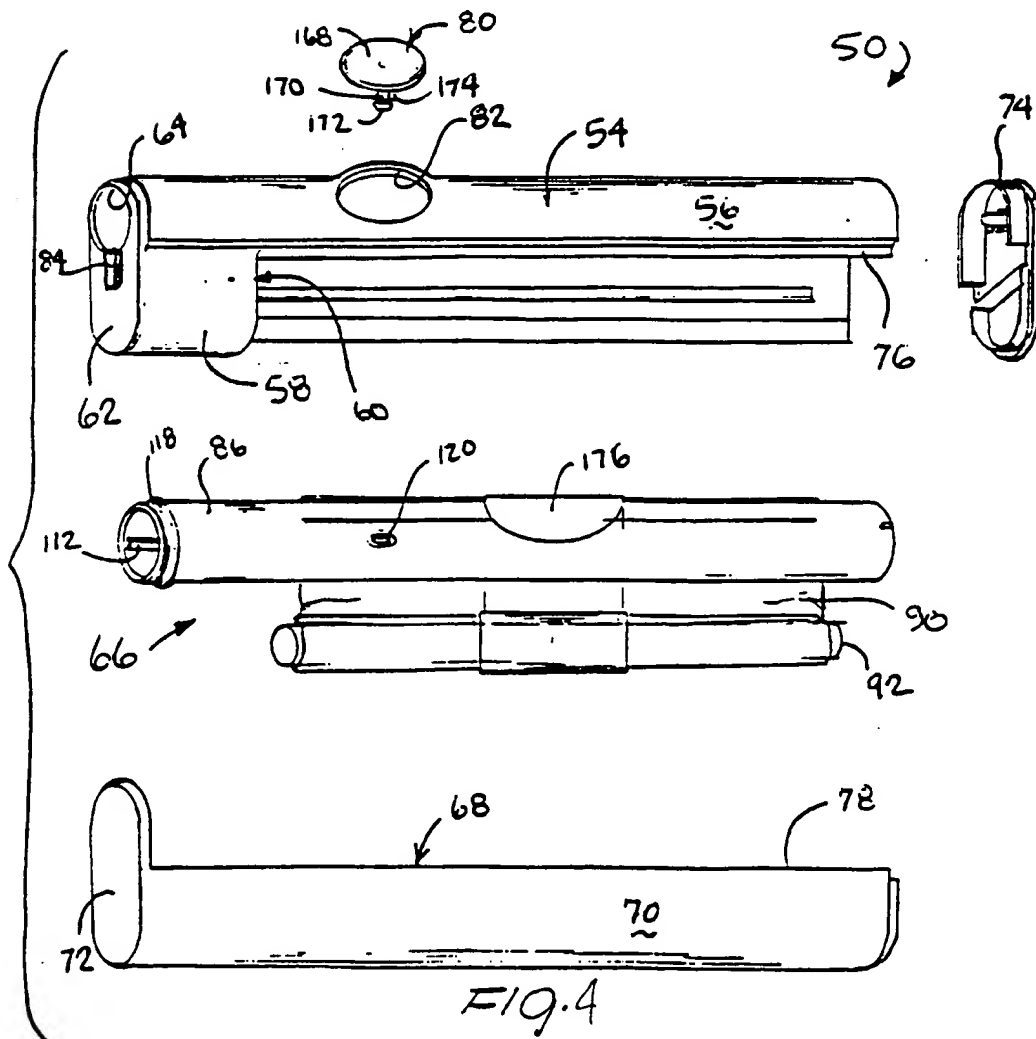
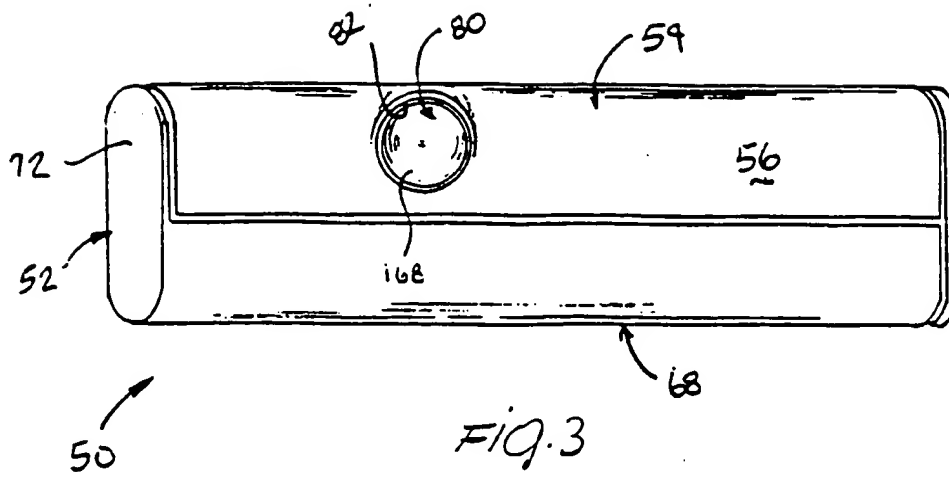
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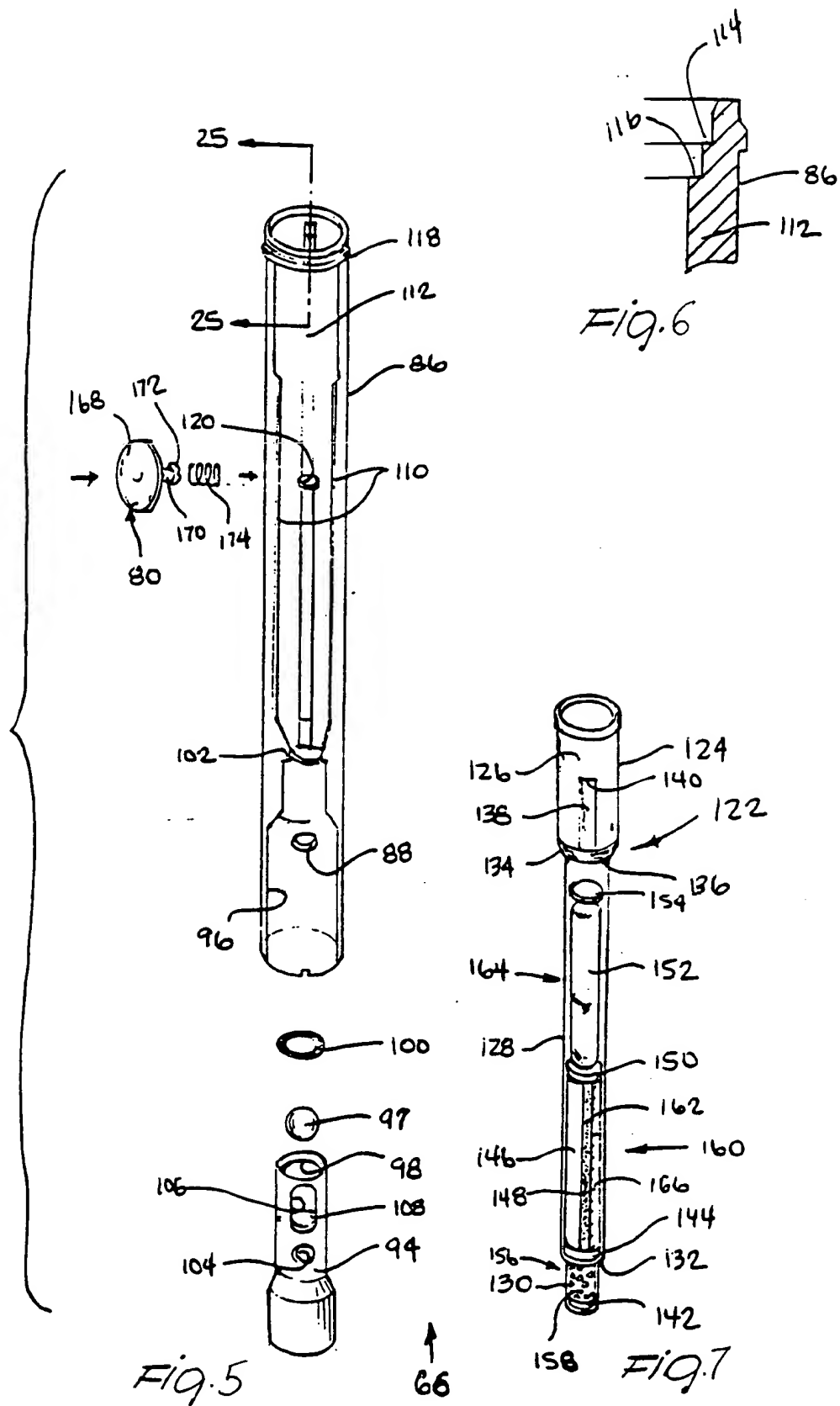
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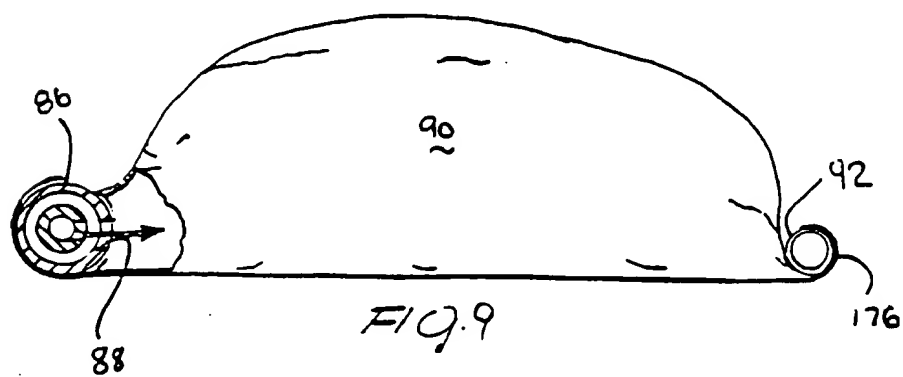
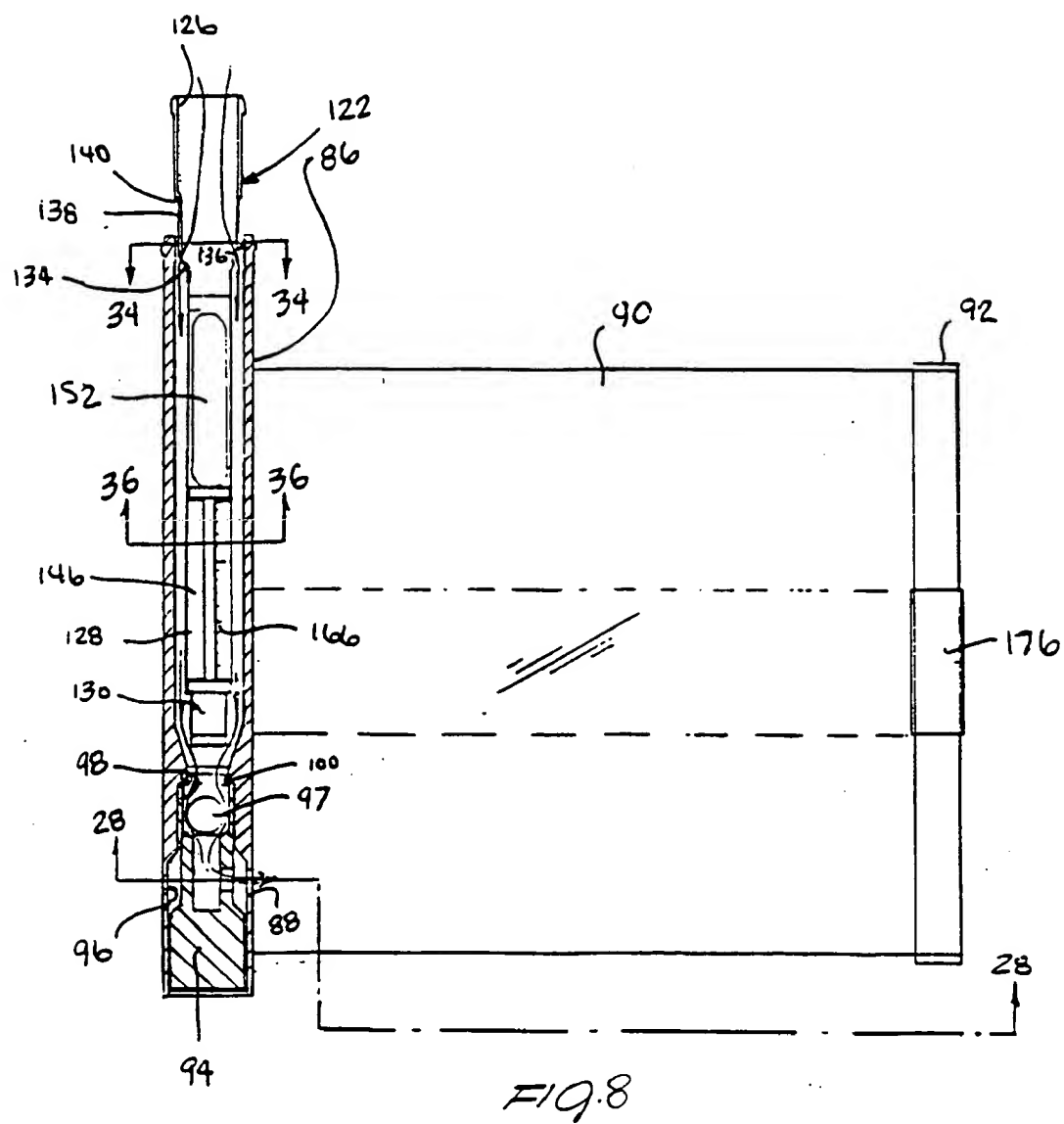
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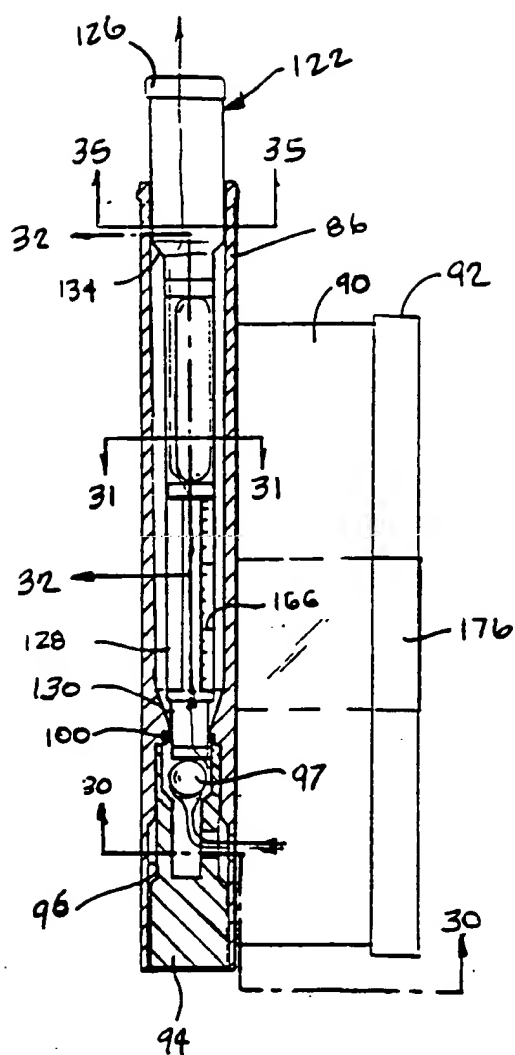


FIG. 10

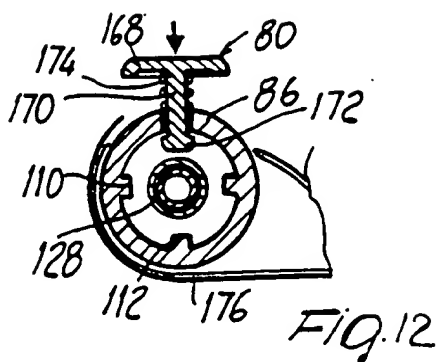


FIG. 12

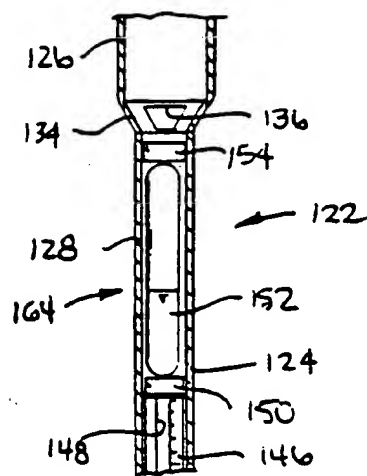


FIG. 13

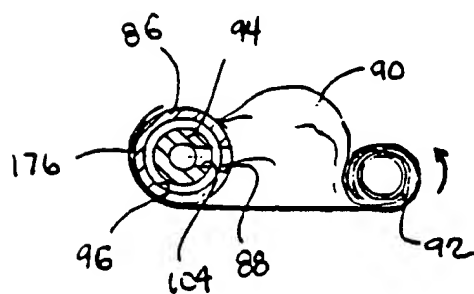


FIG. 11

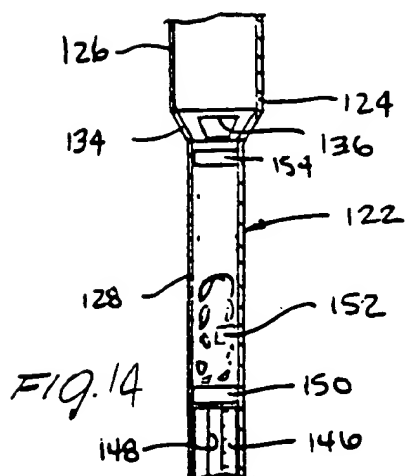


FIG. 14

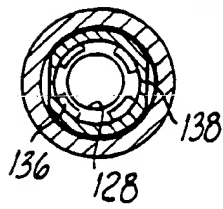
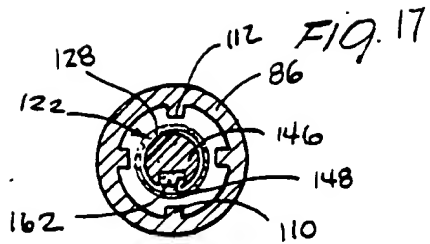


FIG. 15

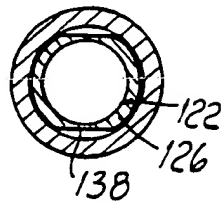


FIG. 16

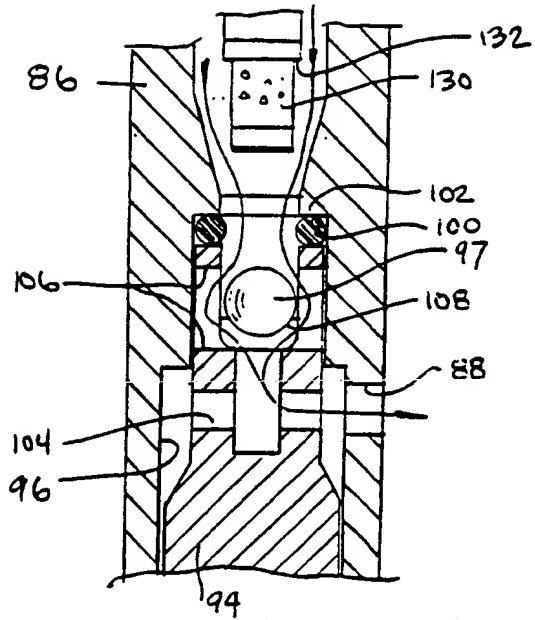


FIG. 18

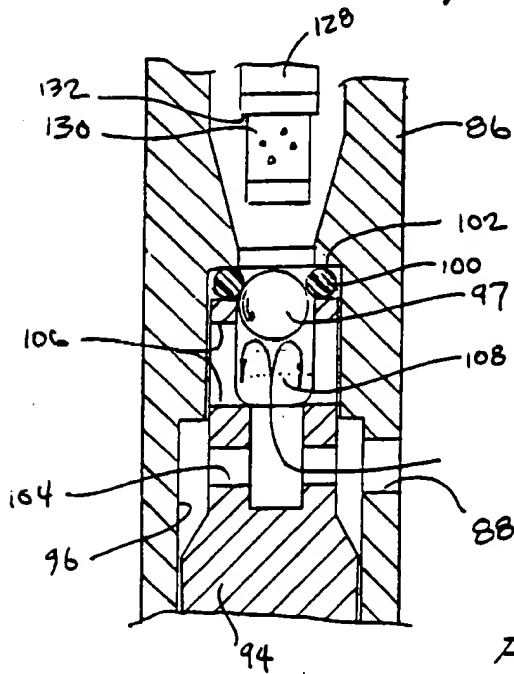


FIG. 19

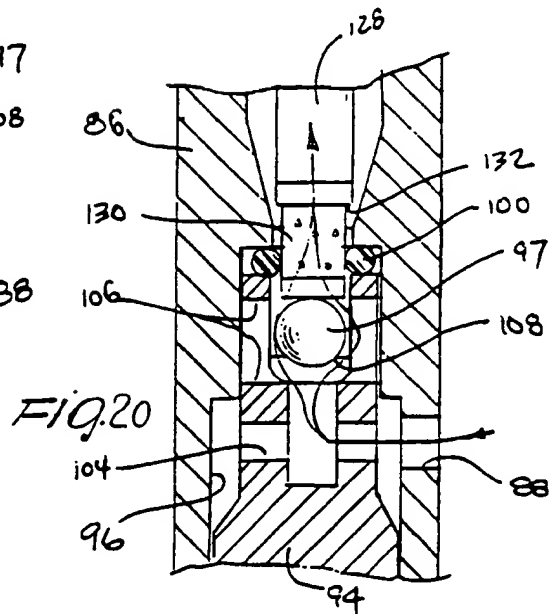


FIG. 20

(19)



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(54) **Breath-sampling device for measuring breath component levels.**

(57) The present invention relates to devices, kits and disposable columns for use in such kits for monitoring levels of various components in the breath of a user. The device generally comprises a) an outer tubular member (86) having an open first end and a second end; b) valve means (94,97) disposed toward the second end of said outer tubular member; c) a breath sample collection means having one end mounted on said tubular member and having the other end closed, and having an interior in communication with the inside of said outer tubular member (86) through said valve means (94,97); and d) a disposable tubular analyzer column (122) having a mouthpiece (126) and containing material reactive to the presence of said breath components, wherein said column (122) is insertable into said outer tubular member (86) and cooperates with said valve means (94,97) to permit breath blown by a user to pass through the outer tubular member (86) into said sample collection means and to permit said collected breath sample to discharge through the reactive material of said analyzer column (122).

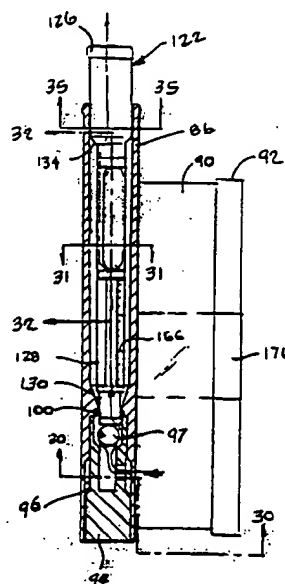


FIG. 10

EP 0 598 262 A3



European Patent  
Office

## EUROPEAN SEARCH REPORT

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EP 93 11 7482

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.4)
X	DE-A-19 48 043 (MINE SAFETY APPLIANCES COMPANY)  * the whole document * ----	1,3, 7-10, 12-14	G01N33/497 G01N33/64 G01N33/98
X	US-A-4 492 673 (W.R.ERIKSEN ET AL.)  * the whole document * ----	1,2,7,8, 12,13,15	
X	US-A-3 676 073 (M.J.LUCKEY) ----	1	
X,D	US-A-4 579 826 (C.E.BOLTON ET AL.) * the whole document * ----	1,2,8,12	
A	DE-A-31 40 883 (MINE SAFETY APPLIANCES CO.) * page 6, line 21 - line 36 * ----	1,9,13, 14	
A	EP-A-0 133 326 (DIVERSIFIED MEDICAL TECHNOLOGIES, INC.) * page 5, line 10 - page 8, line 29; figures 1-4 * -----	13-15	
			TECHNICAL FIELDS SEARCHED (Int.Cl.4)
			G01N A61B
The present search report has been drawn up for all claims			
Place of search BERLIN		Date of completion of the search 1 August 1994	Examiner De Kok, A
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	